CASE REPORT | OPEN ACCESS

Medical Science

Asymmetrical face while crying in pediatrics: Cayler syndrome

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To Cite:
Almohammal MN, Alqarni SA, Alqarni A, Alaklabi SNA, Alshahrani NA, Algarni AAM. Asymmetrical face while crying in pediatrics: Cayler syndrome. *Medical Science* 2024; 28: e67ms3310
doi: https://doi.org/10.54905/disssi.v28i148.e67ms3310

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Peer-Review History
Received: 09 April 2024
Reviewed & Revised: 13/April/2024 to 17/June/2024
Accepted: 21 June 2024
Published: 27 June 2024

Peer-review Method
External peer-review was done through double-blind method.

Medical Science
pISSN 2321–7359; eISSN 2321–7367

ABSTRACT

Cayler syndrome is a rare pediatric condition characterized by asymmetric crying faces and various associated anomalies. This case series study presented five cases of Cayler syndrome, with the aim of contributing to the growing body of knowledge about this condition. The study observed that Cayler syndrome has a wide range of clinical presentations and associated anomalies, highlighting the complexity of the condition. Recognizing the various phenotypic expressions of the syndrome is crucial to ensure timely and appropriate care. The study also observed familial cases of Cayler syndrome. Further research is needed to explore the genetic basis of Cayler syndrome, as identifying potential causative genetic mutations could improve the accuracy of diagnosis and provide information for genetic counseling. Furthermore, the study found a strong association between Cayler syndrome and congenital heart defects, emphasizing the need for a rigorous cardiac evaluation in infants with suspected or confirmed cases.

Keywords: Asymmetric crying faces, clinical presentations, congenital heart defects, genetic basis, pediatric condition

1. INTRODUCTION

Cardio-facial syndrome was first described by (Cayler, 1969). Congenital heart disease and crying faces of asymmetrical are seen in this rare pediatric condition (Pawar et al., 2015). In addition to cognitive and behavioral problems that develop over time, it can be linked to abnormalities in the kidney, ENT, digestive system, and joints, as well as hypocalcemia and cellular immune malfunction (Alaoui et al., 2022). Cayler syndrome is also known as 'Asymmetric crying faces with cardiac defects or hypoplasia of the depressor anguli oris muscle with cardiac defects' (Pawar et al., 2015).

It presents with a notable unilateral depression of the lower lip during crying that is observed within the first few weeks after giving birth, whereas bilaterally intact forehead wrinkles, depth of the nasolabial fold, and closure of the eyelid closure are all present (Pasick et al., 2013). In Cayler's cardio-facial syndrome,

hypoplasia of the depressor anguli oris muscle leads to the failure of one side of the mouth to move outward and downward while crying or grimacing (Bawle et al., 1998). Heterogenic causes can lead to Cayler syndrome. It might manifest as a sporadic autosomal dominant characteristic or as deletions of chromosome 22q11.2 (Bawle et al., 1998). In the study, we aim to shed light on 8 cases of Cayler syndrome, which is considered an uncommon condition.

2. MATERIALS AND METHODS

We reported 5 cases with Cayler syndrome, taken from Maternity and Children's Hospital, Bisha city, Kingdom of Saudi Arabia. The cases were obtained from medical records, pictures, and videos performed with informed consent.

Case Presentation 1

A term male baby was born to the non-consanguineous couple through standard vaginal delivery with a birth weight of 2.5 kg. The baby had a normal Apgar score of 7/8/9. The antenatal scan was standard, and the mother had a known case of hypothyroidism and was on Eltroxin treatment. This was a spontaneous conception. The postnatal course of the baby was uneventful. At birth, the baby was diagnosed to have asymmetric crying faces with a deviation of the angle of the mouth to the right side (Figure 1). The baby had regular faces while sleeping or silent. There was no abnormality in closing their eyes while sleeping. There was no cutaneous marker or any prominent malformation on the lip and palate. There was no hemifacial microsomia, epi-bulbar dermoid, or other paralysis of the cranial nerve (ruling out Goldenhar, Moebius, and craniofacial microsomia). There was a family history of the same presentation in his older brother and no other complaints and the examination of the parents was regular.

The baby was investigated with an echocardiogram, brain ultrasound, whole-body X-ray, whole spine lateral X-ray column, and fundus examination. The echocardiogram showed a muscular ventricular septal defect; the brain ultrasound was normal, and the fundus examination was normal. Routine blood investigation showed normal calcium and other minerals, and total body radiographs were also normal. Examination and X-ray of the cervicothoracic vertebral column X-ray were not suggestive of any skeletal abnormalities that rule out Goldenhar syndrome. The baby was not genetically investigated. Eye exam, hearing test, immunology tests, and renal ultrasound of the infant were normal. The infant was discharged and is now under follow-up.

Figure 1 Asymmetric crying faces with a deviation of the angle of mouth to the right (Video available at: https://youtube.com/shorts/T0prfXZIn20?si=KcDknihyjBIn_m2P) (Source: Authors work)

Case presentation 2

The 5-year-old boy was referred from the nephrology clinic as a case of bilateral polycystic kidney disease with facial asymmetry; this patient was full term, born to nonconsanguineous parents, through normal vaginal delivery with a birth weight of 2.8 kg. The baby had a normal Apgar score of 7/8/9. The antenatal scan was normal and the mother was medically free. This was a spontaneous conception. The postnatal course of the baby was uneventful. At birth, the baby was diagnosed with bilateral hydronephrosis but regarding facial asymmetry only the mother noticed this abnormality and she did not seek medical advice at the age of 5 years his nephrologist noticed that and referred him to my clinic as a case of asymmetric crying and a deviation of the mouth angle to the right side (Figure 2).

The baby had normal faces while sleeping or silent. There was no abnormality in closing eyes while sleeping. There was no cutaneous marker or any obvious malformation on the lip and palate. There was no hemifacial microsomia, no epibulbar dermoid, or other paralysis of the cranial nerve (ruling out Goldenhar, Moebius, and craniofacial microsomia). There was no family history of illness and no other complaints and the examination of parents was normal. The patient was investigated with an echocardiogram, brain CT, whole-body X-ray, whole spine lateral X-ray column, and fundus examination. The echocardiogram showed a small patent ductus arteriosus (PDA), the brain CT was normal, and the fundus examination was normal.

The blood investigation showed normal calcium and other minerals, and there were also normal total body radiographs. Examination and X-ray of the cervicothoracic vertebral column X-ray were not suggestive of any skeletal abnormalities that rule out Goldenhar syndrome. The patient was not genetically investigated. An eye exam, hearing test, immunology tests, and renal ultrasound of the patient showed a bilateral polycystic kidney with normal renal function test. The patient was diagnosed with Cayler syndrome and is now being followed.

Figure 2 Asymmetric crying faces with a deviation of angle of mouth to Right (Video available at: https://youtube.com/shorts/PNxI_HGgVcU?si=U7tssMt7aSAVnjMn) (Source: Authors work)

Case presentation 3

A post term (41weeks) girl baby was born to a non-consanguineous couple, through normal vaginal delivery with birth weight of 4 kg. The baby had a normal Apgar score of 7/8/9. The prenatal scan was normal, and the mother was unknown to have any medical

conditions. This was a spontaneous conception. The postnatal course of the baby was uneventful. At birth, the baby was diagnosed to have asymmetric crying faces with a a deviation of angle of mouth to left by (Figure 3). Baby had normal faces while sleeping or silent. There was no abnormality in closing eyes while sleeping. There was no cutaneous marker or obvious malformation in the cleft lip and palate except microtia of the right ear. There was no hemifacial microsomia, no epibulbar dermoid or other paralysis of the cranial nerve (ruling out Goldenhar, Moebius and craniofacial microsomia). There was no family history and the examination of the parents was normal.

The baby was investigated with echocardiogram, brain ultrasound, and whole-body X-ray, whole spine lateral X-ray column and fundus examination. The echocardiogram showed a small PDA; brain ultrasound was normal and fundus examination did not show any abnormalities. Routine blood investigation showed normal calcium and normal TSH. The total body X-ray examination and X-ray of the cervico-thoracic vertebral column X-ray were not suggestive of any skeletal abnormalities that rule out Goldenhar syndrome. Eye exam, hearing test, immunology tests, and renal ultrasound of the infant were normal. The infant was discharged and is now under follow-up.

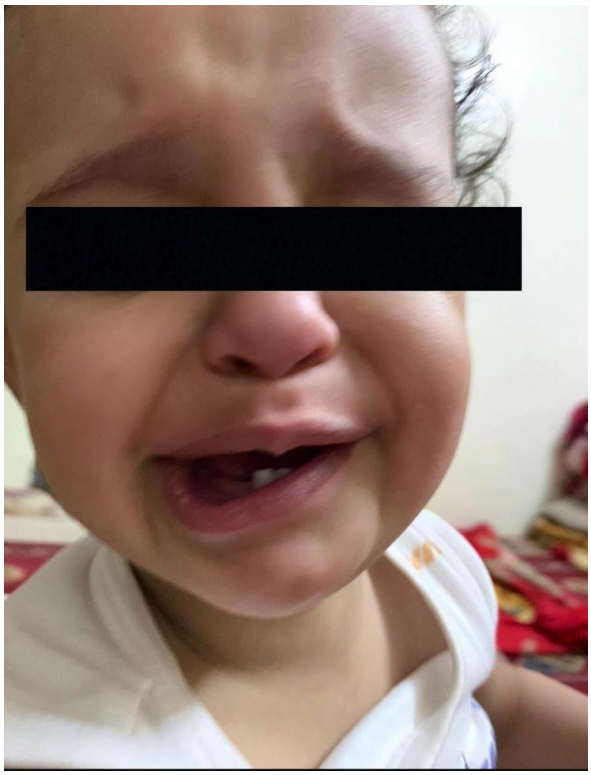

Figure 3 Asymmetric crying faces with a deviation of the angle of mouth to the right

Case presentation 4

A term male baby was born to a nonconsanguineous couple through normal vaginal delivery with normal weight. The baby had a normal Apgar score of 7/8/9. The prenatal scan was normal, and the mother was unknown to have any medical conditions; the postnatal course of the baby was uneventful. At birth, the baby was diagnosed to have asymmetric crying faces with a deviation of the angle of the mouth to the right side (Figure 4). The baby had normal faces while sleeping or silent. There was no abnormality in closing eyes while sleeping. There was no cutaneous marker or any obvious malformation on the lip and palate. There was no hemifacial microsomia, no epibulbar dermoid, or other paralysis of the cranial nerve (ruling out Goldenhar, Moebius, and craniofacial microsomia). There was a family history of the same presentation in his nieces (case presentation 5), and there was no other complaint, and the examination of the parents was normal.

The baby was investigated with an echocardiogram, brain ultrasound, whole-body X-ray, whole spine lateral X-ray column, and fundus examination. The echocardiogram showed a muscular ventricular septal defect; the brain ultrasound was normal, and the fundus examination was normal. The blood investigation showed normal calcium and other minerals, and there were also normal total body radiographs. Examination and X-ray of the cervicothoracic vertebral column X-ray were not suggestive of any skeletal abnormalities that rule out Goldenhar syndrome. The baby was not investigated genetically investigated. Eye exam, hearing test, immunology tests, and renal ultrasound of the infant were normal. The infant was discharged and is now under follow-up.

Figure 4 Asymmetric crying faces with a deviation of angle of mouth to Right

Case presentation 5

A full-term (39 weeks) girl baby was born to a non-consanguineous couple through normal vaginal delivery with a birth weight of 3 kg. The baby had a normal Apgar score of 7/8/9. The prenatal scan was normal, and the mother had no medical conditions. This was a spontaneous conception. The postnatal course of the baby was uneventful. At birth, the baby was diagnosed to have asymmetric crying faces with a deviation of the angle of the mouth to the left (Figure 5). The baby had normal faces while sleeping or silent. There was no abnormality in closing eyes while sleeping. There was no cutaneous marker or obvious malformation in the cleft lip and palate except the microtia of the right ear. There was no hemifacial microsomia, no epibulbar dermoid, or other paralysis of the cranial nerve (ruling out Goldenhar, Moebius, and craniofacial microsomia). There was a family history of the same presentation in his niece (case presentation 4), and there is no other complaint, and the examination of the parents was normal.

The baby was investigated with an echocardiogram, brain ultrasound, whole-body X-ray, whole spine lateral X-ray column, and fundus examination. The echocardiogram showed a small PDA; the brain ultrasound was normal, and the fundus examination showed tortuous no abnormality. Blood investigation showed normal calcium and normal TSH. The total body X-ray examination and X-ray of the cervicothoracic vertebral column X-ray were not suggestive of any skeletal abnormalities that rule out Goldenhar syndrome. Eye exam, hearing test, immunology tests, and renal ultrasound of the infant were normal. The infant was discharged and is now under follow-up.

Figure 5 Asymmetric crying faces with a deviation of angle of mouth to Right (Video available at: https://youtube.com/shorts/qbfDamZ_ZwI?si=SfKfKdGvgOYdHYDV) (Source: Authors work)

3. DISCUSSION

Cayler syndrome, characterized by asymmetric crying faces and various associated anomalies, remains a rare but exciting pediatric condition that has attracted the attention of the medical community in recent years. Our study aimed to contribute to the growing body of knowledge on Cayler syndrome by presenting 5 cases of this condition. The variability in the presentation of Cayler syndrome, ranging from the extent of facial asymmetry to the presence of associated anomalies, emphasizes the complexity of the condition. The clinical heterogeneity observed in our case reports is consistent with the findings from (Pawar et al., 2015). The clinical implications of this heterogeneity are profound, as they underscore the challenge for healthcare providers in diagnosing Cayler syndrome solely based on clinical presentation (Robin et al., 2005).

Recognition of the various phenotypic expressions of the syndrome is vital to ensure that patients receive timely and appropriate care. Our study's observation of familial cases aligns with previous studies, suggesting a possible genetic predisposition to Cayler Syndrome. Identifying potential causative genetic mutations is imperative for several reasons. First, it could lead to a more accurate diagnosis, helping healthcare providers confirm the condition and allowing early intervention. Second, understanding the genetic mechanisms could offer insights for genetic counseling and help families make informed decisions about future pregnancies. Cardiac abnormalities, such as muscular ventricular septal defects and patent ductus arteriosus (PDA), were common among the cases, consistent with the findings of (Kumar et al., 2020). The strong association between Cayler Syndrome and congenital heart defects underscores the need for a rigorous cardiac evaluation in infants with suspected or confirmed cases.

The clinical significance of these cardiac abnormalities cannot be overstated. Early cardiac evaluation is crucial to detect and manage congenital heart defects promptly. Collaboration between pediatric cardiologists and other specialists is essential to ensure comprehensive care for these patients. Effective coordination between healthcare providers can significantly improve the overall outcome for these children. In particular, none of the cases in our study presented craniofacial microsomia, epibulbar dermoid, or

paralysis of the cranial nerve, contrasting with conditions such as Goldenhar Tuin et al., (2015) and Moebius syndromes (Chowdhury et al., 2020). This absence of these characteristic features is a hallmark of Cayler Syndrome (Pawar et al., 2015). The lack of these characteristics serves as a distinctive clinical indicator, helping healthcare providers differentiate Cayler syndrome from other craniofacial conditions.

Recognizing these unique characteristics is critical in guiding the diagnostic process and ensuring patients receive the most appropriate care. Our study underscores the importance of early recognition of Cayler syndrome, a sentiment shared by (Gerdes et al., 2001). Some of our cases were diagnosed only after a delay in seeking medical attention, highlighting the critical importance of early recognition. Detection and timely diagnosis are essential for appropriate care and intervention for associated abnormalities, including cardiac defects and renal problems. Multidisciplinary care, including pediatricians, cardiologists, geneticists, and other specialists, is crucial in the treatment of the complex medical needs of individuals with Cayler Syndrome (Óskarsdóttir et al., 2023). It ensures that these patients receive comprehensive care customized to their unique clinical presentations.

4. CONCLUSIONS

This present case report study sheds light on the clinical diversity of Cayler syndrome, emphasizing the importance of early recognition, diagnosis, and multidisciplinary care. The clinical heterogeneity observed and familial occurrences suggest possible genetic underpinnings that need to be explored. Cardiac anomalies were shared among our cases, highlighting the need for cardiac evaluation for timely intervention.

Authors' Contributions

The collaborative effort of this research project involved contributions from various team members. Mohammad N Almohammal took the lead in data collection, ensuring a comprehensive and reliable data set for the study. Saad Ali Alqarni played a crucial role in designing the overall framework of the work, laying the foundation for a structured and coherent approach. The interpretation of findings was skillfully handled by Anas Alqarni, whose insights added depth to the discussion. The critical aspects of manuscript writing and editing were spearheaded by Saeed Naseer A Alaklabi and Nasser Ali Alshahrani, both of whom contributed their expertise to refine the narrative and ensure clarity. Serving as the guarantor of the study, Mohammad N Almohammal assumed responsibility for the integrity and precision of the research process.

Informed Consent

Informed consent was obtained from all subjects (parents or guardians of minors) involved in the study.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

Data supporting this study's findings are available from the corresponding author (Saad A Alqarni) upon reasonable request.

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